

limitations of the product of Group I, and must thus be rejoined upon allowance of the claims of Group I. Accordingly, Applicants respectfully request reconsideration and withdrawal of the Restriction Requirement.

II. Rejection Under §103

Claims 1, 3-17 and 59-71 are rejected under 35 U.S.C. §103(a) over Clark in view of Kronenthal, Banitt, Collins, and EP 623 and further in view of Hammerslag. The Office Action argues that the claimed invention would have been obvious over the cited references. Applicants respectfully traverse this rejection.

A. The Claimed Invention

The claimed invention is generally directed to biocompatible adhesive compositions, methods of treating tissue using such compositions, and kits containing such compositions. In particular, claim 1 is directed to a biocompatible adhesive composition, comprising: a first monomer species; and a second monomer species different from said first monomer species, wherein at least said first monomer species is absorbable, an absorption rate of said first monomer species is different from an absorption rate of said second monomer species, and wherein said first monomer species comprises an alkyl ester cyanoacrylate. Independent claim 59 is directed to a biocompatible adhesive composition, comprising: at least one alkyl ester cyanoacrylate monomer; a second monomer species having an absorption rate different from an absorption rate of said at least one alkyl ester cyanoacrylate monomer; and a polymerization initiator or accelerator, wherein said polymerization initiator or accelerator is a quaternary amine.

Thus, each of independent claims 1 and 59 specifically requires the presence of an alkyl ester cyanoacrylate as the first monomer species, and a second monomer species that is different from the alkyl ester cyanoacrylate and has a different absorption rate. According to the claimed invention, the combination of a faster absorbing monomer species and non-

absorbable (or less absorbable or slower absorbing) monomer species allows for adjustment and tailoring of the degradation rate of the resultant formed polymer. Example 6 in the specification, at pages 25-26, demonstrates that at varying percentages of two different polymerizable monomers, the biodegradation rate of the resultant polymer composition is varied.

Such a composition, and related methods and kits, were heretofore unknown in the art, and provides significant advantages for future uses.

B. Clark Does Not Teach or Suggest the Claimed Invention

Clark is directed to an applicator tip for dispensing a polymerizable and/or cross-linkable material which is porous, absorbent or adsorbent and includes a polymerization or cross-linking initiator. The initiator initiates polymerization or cross-linking when the polymerizable and/or cross-linkable material is dispensed through the applicator tip. The polymerizable and/or cross-linkable material may be applied to a variety of substrates. See Clark at Abstract.

The Office Action correctly points out that Clark discloses the use of various cyanoacrylate monomers. However, Clark nowhere specifically discloses, and entirely fails to teach or suggest, the use of alkyl ester cyanoacrylates, as specifically required by the claimed invention, in combination with a second, different monomer species that has an absorption rate that is different from the alkyl ester cyanoacrylate.

1. Clark Does Not Teach the Specific Claimed Alkyl Ester Cyanoacrylate

As described above, each of independent claims 1 and 59 specifically require the presence of a first monomer species, which is an alkyl ester cyanoacrylate monomer. However, Clark nowhere teaches or suggests the specific claimed alkyl ester cyanoacrylate monomer, and thus cannot have rendered obvious the claimed invention.

Clark specifically discloses a number of suitable monomers, including specific suitable cyanoacrylate monomers, but fails to disclose the specific alkyl ester cyanoacrylates from within the generic group of cyanoacrylates. With respect to the monomers, Clark discloses that the monomers may suitably be selected from 1,1-disubstituted monomers of the formula $\text{CHR}=\text{CXY}$. See col. 4, lines 35-44. Clark goes on to disclose that preferred and "especially advantageous" monomers are the cyanoacrylates, including those of formula (II). See col. 4, line 52 to col. 5, line 12. At most, the disclosure of Clark only broadly encompasses the alkyl ester cyanoacrylates. However, alkyl ester cyanoacrylates are obtained from the broad disclosure of Clark only if the substituents R^3 , R^7 and R^8 are properly and narrowly selected from among their broad disclosed scope. Clark nowhere specifically teaches selecting each of R^3 , R^7 and R^8 in a manner to properly provide an alkyl ester cyanoacrylate, as claimed.

Still further, Clark discloses preferred monomers to include alkyl alpha-cyanoacrylates, such as 2-octyl cyanoacrylate. Col. 5, lines 33-39. Clark thus teaches away from selecting alkyl ester cyanoacrylates, from the broad monomer disclosure, and teaches that alkyl alpha-cyanoacrylates are instead preferred.

Accordingly, Clark does not disclose, teach or suggest specific examples of the alkyl ester cyanoacrylates. Nor does Clark teach or suggest any preference for one monomer over the rest, except perhaps for the use of alkyl alpha cyanoacrylates, and by no means discloses or suggests any preference for alkyl ester cyanoacrylates, which are not specifically disclosed in the reference. Although the disclosure of Clark may broadly encompass the various specific monomer components of the claimed invention individually, Clark would not have rendered obvious the claimed invention. The reference thus cannot have rendered obvious the claimed invention.

2. Clark Does Not Teach the Claimed Combination of Monomers

Still further, Clark nowhere teaches or suggests that any such specifically selected cyanoacrylate monomer should specifically be used in combination with a second, different monomer species, as claimed. Clark entirely fails to disclose the combined use of the two different monomer species, as claimed.

As described above, each of independent claims 1 and 59 specifically require the presence of two different monomer species, one of which is the above-described alkyl ester cyanoacrylate monomer. However, Clark nowhere teaches or suggests the specific claimed combined use of an alkyl ester cyanoacrylate monomer and a second monomer species, and thus cannot have rendered obvious the claimed invention.

Just as Clark does not teach or suggest the required alkyl ester cyanoacrylate, so too does Clark fail to disclose, teach or suggest the combined use of two or more monomer species, having different absorption rates, in any combination, much less in the combination required by the present independent claims. Just as Clark does not teach or suggest any preference for one monomer over the rest, and does not teach or suggest the specific alkyl ester cyanoacrylates, so too does Clark not teach or suggest the use of two different monomer species having different absorption rates, as claimed.

In the present case, Clark fails to teach or suggest specifically selecting the alkyl ester cyanoacrylate monomer and a second, different monomer having a different absorption rate, as claimed. Clark only broadly encompasses the use of various cyanoacrylate monomers, but does not teach the combined use of two different monomers. In the absence of any such teachings, the reference cannot have rendered obvious the claimed invention.

C. The Secondary References Fail to Overcome Clark's Deficiencies

Furthermore, none of the secondary references, alone or in combination, overcome the above-described deficiencies of Clark, whether alone or in combination.

Kronenthal is cited for its disclosure of carbalkoxyalkyl 2-cyanoacrylates, which are disclosed to be readily assimilated by tissues and exhibit a relatively low degree of inflammatory tissue response. However, Kronenthal fails to disclose, teach or suggest that one of ordinary skill in the art should select two different monomer species, each having different absorption rates, for use in a biocompatible adhesive composition, as claimed. At most, one of ordinary skill in the art might have been motivated to modify Clark by using only the carbalkoxyalkyl 2-cyanoacrylate of Kronenthal. However, such a modification still would not have yielded the claimed invention. Any combination of Clark and Kronenthal would still thus not have included a mixture of two different monomer species, as claimed.

Banitt is cited for its disclosure of alkoxyalkyl 2-cyanoacrylates, which are disclosed to be biodegradable and of minimal toxicity. However, Banitt, like Kronenthal above, fails to disclose, teach or suggest that one of ordinary skill in the art should select two different monomer species, each having different absorption rates, for use in a biocompatible adhesive composition, as claimed. At most, one of ordinary skill in the art might have been motivated to modify Clark by using only the alkoxyalkyl 2-cyanoacrylate of Banitt. However, such a modification still would not have yielded the claimed invention. Any combination of Clark, Kronenthal and Banitt would still thus not have included a mixture of two different monomer species, as claimed.

Collins is cited for its disclosure that octyl 2-cyanoacrylate is a more effective tissue adhesive. Collins is further cited for its alleged teaching that a composition is desired having the low toxicity and fast polymerization rate of the higher homolog cyanoacrylates, and the biodegradability of methyl cyanoacrylate. However, Collins likewise fails to disclose, teach or suggest that one of ordinary skill in the art should select two different monomer species, each having different absorption rates, for use in a biocompatible adhesive composition, as claimed. In fact, when considered in combination with Clark, Kronenthal and Banitt, Clark and Collins

appear to be directly contradictory to Kronenthal and Banitt. Each of Clark and Collins express a distinct preference for alkyl alpha-cyanoacrylates, whereas Kronenthal and Banitt express a preference for carbalkoxyalkyl 2-cyanoacrylate (Collins) or alkoxyalkyl 2-cyanoacrylates (Banitt). Accordingly, one of ordinary skill in the art would at best have been motivated to use either the monomers of Clark and/or Collins, or the monomers of Kronenthal or Banitt, but not a combination of them in a single composition. Any combination of the references thus would still not have provided the claimed invention.

In fact, Applicants submit that the contradictory teachings of Clark and Collins as compared to Kronenthal and Banitt, demonstrates that the asserted combination of the four references is improper. In order to combine the cited references, there must be some demonstrated motivation to do so, either in the references themselves or elsewhere in the art. However, no such motivation has been shown to combine the four cited references. Thus, the combination is both improper, and nevertheless does not provide the claimed invention.

EP 623 is cited for its disclosure of stabilizing agents, and thus is cited for limitations of dependent claims. However, this reference does not overcome the above-described deficiencies of the primary references as they relate to the independent claims. Accordingly, any combination of EP 623 with the remaining references would not have rendered obvious the claimed invention.

D. Hammerslag Teaches Away from the Claimed Invention

Furthermore, the Office Action cites Hammerslag to support the rejection. However, any combination of Hammerslag with the remaining references is both improper, and would not have rendered obvious the claimed invention.

The Office Action cites that Hammerslag for the assertions that cyanoacrylates have varying biodegradation rates, and that the biodegradation rate of the cyanoacrylate can be altered

as desired. However, while Hammerslag may teach biodegradation variation, Hammerslag in fact teaches away from the claimed invention.

The Office Action cites to Hammerslag at col. 5, lines 21-33 for the teaching of varying biodegradation. However, in that passage, Hammerslag only teaches that the biodegradation can be varied by cross-linking a polymer product into the cyanoacrylate adhesive. For example, Hammerslag teaches that biodegradation can be varied by cross-linking a polyacrylic acid having a molecular weight of 200,000-600,000 to the cyanoacrylate to form a final compound. Nowhere does Hammerslag teach or suggest that the biodegradation rate could or should be varied by means of a biocompatible adhesive composition, comprising: a first monomer species and a second monomer species different from said first monomer species, wherein at least said first monomer species is absorbable, and an absorption rate of said first monomer species is different from an absorption rate of said second monomer species, and wherein said first monomer species comprises an alkyl ester cyanoacrylate, as claimed.

Because Hammerslag teaches incorporating a polymer product, rather than a second monomer species, into the composition to vary its biodegradation rate, Hammerslag actually teaches away from the claimed invention. Hammerslag does not teach or suggest that the biodegradation rate can be varied by using two different monomer species in the composition, as claimed.

E. Conclusion

Accordingly, considering the cited references in combination, one of ordinary skill in the art would not have been motivated to practice the claimed invention. The cited references fail to teach or suggest selecting a plurality of different monomer species, having different absorption rates, where the first monomer species is an alkyl ester cyanoacrylate as claimed.

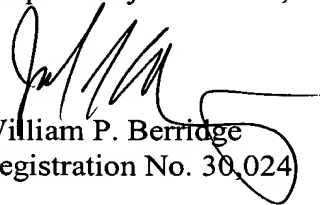
The claimed invention is thus patentable over the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

III. Conclusion

In view of the foregoing remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of the application are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,



William P. Berridge
Registration No. 30,024

Joel S. Armstrong
Registration No. 36,430

WPB:JSA

Date: March 29, 2004

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

<p>DEPOSIT ACCOUNT USE AUTHORIZATION Please grant any extension necessary for entry; Charge any fee due to our Deposit Account No. 15-0461</p>
--